AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method of assessing a combinatorial library for complementarity to a target of known three-dimensional structure, having at least one binding site ~~of known geometry~~, said combinatorial library comprising a plurality of ligands, each based on a common core, said method comprising:

docking each ligand of said plurality of ligands to the target molecule to generate a plurality of ligand positions relative to the target molecule in a plurality of ligand-target molecule complex formations, said plurality of ligand positions comprising a plurality of common core positions relative to the target molecule;

determining the rms (root mean square) deviation of one or more common core positions of said plurality of common core positions from one or more other common core positions of said plurality of common core positions; ~~and~~

forming clusters of ligands from said plurality of ligands according to said rms (root mean square) deviation~~.~~; and

rating complementarity of the combinatorial library to the target molecule based on the clusters formed.

2. (Currently amended) A method according to claim 1, ~~additionally comprising~~wherein rating the complementarity of the combinatorial library to the target molecule ~~according to~~is based on the number of ligands in a cluster having a minimum rms (root mean square) deviation relative to the number of ligands in the combinatorial library.

3. (Currently amended) A method according to claim 1 wherein said determining the rms (root mean square) deviation comprises:

placing a grid around a binding site of the target molecule;

for each ligand position, determining a location on the grid corresponding to the center of mass of the common core; and

determining the rms (root mean square) deviation of each common core position from every other common core position having a location on the grid within a predetermined distance.

4. (Original) A method according to claim 1 wherein said forming clusters comprises forming clusters using a single linkage clustering algorithm.

5. (Previously presented) A method according to claim 1 wherein said docking each ligand comprises:

performing a conformational search to generate multiple solution conformations of each ligand;

generating a binding site image of the target molecule, said binding site image comprising multiple hot spots;

matching hot spots of the binding site image to atoms in at least one solution conformation of the multiple solution conformations of each ligand to obtain at least one ligand position relative to the target molecule in a ligand-target molecule complex formation; and

optimizing the at least one ligand position while allowing translation, orientation and rotatable bonds of the ligand to vary, and while holding the target molecule fixed.

6. (Currently amended) A system for assessing a combinatorial library for complementarity to a target of known three-dimensional structure, having at least one binding site ~~of known geometry~~, said combinatorial library comprising a plurality of ligands, each based on a common core, said system comprising:

means for docking each ligand of said plurality of ligands to the target molecule to generate a plurality of ligand positions relative to the target molecule in a plurality of ligand-target molecule complex formations, said plurality of ligand positions comprising a plurality of common core positions relative to the target molecule;

means for determining the rms (root mean square) deviation of one or more common core positions of said plurality of common core positions from one or more other common core positions of said plurality of common core positions; ~~and~~

means for forming clusters of ligands from said plurality of ligands according to said rms (root mean square) deviation.; and

means for rating complementarity of the combinatorial library to the target molecule based on the clusters formed.

7. (Currently amended) A system according to claim 6, ~~additionally comprising~~wherein the means for rating the complementarity of the combinatorial library to the

target molecule ~~according to~~is based on the number of ligands in a cluster having a minimum rms (root mean square) deviation relative to the number of ligands in the combinatorial library.

8. (Currently amended) A system according to claim 6 wherein said means for determining the rms (root mean square) deviation comprises:

means for placing a grid around a binding site of the target molecule;

means for, for each ligand position, determining a location on the grid corresponding to the center of mass of the common core; and

means for determining the rms (root mean square) deviation of each common core position from every other common core position having a location on the grid within a predetermined distance.

9. (Previously presented) A system according to claim 6 wherein said means for forming clusters comprises means for forming clusters using a single linkage clustering algorithm.

10. (Previously presented) A system according to claim 6 wherein said means for docking each ligand comprises:

means for performing a conformational search to generate multiple solution conformations of each ligand;

means for generating a binding site image of the target molecule, said binding site image comprising multiple hot spots;

means for matching hot spots of the binding site image to atoms in at least one solution conformation of the multiple solution conformations of each ligand to obtain at least one ligand position relative to the target molecule in a ligand-target molecule complex formation; and

means for optimizing the at least one ligand position while allowing translation, orientation and rotatable bonds of the ligand to vary, and while holding the target molecule fixed.

11. (Currently amended) At least one program storage device readable by a machine, tangibly embodying at least one program of instructions executable by the machine to perform a method for assessing a combinatorial library for complementarity to a target of known three-

dimensional structure, having at least one binding site ~~of known geometry~~, said combinatorial library comprising a plurality of ligands, each based on a common core, said method comprising:

docking each ligand of said plurality of ligands to the target molecule to generate a plurality of ligand positions relative to the target molecule in a plurality of ligand-target molecule complex formations, said plurality of ligand positions comprising a plurality of common core positions relative to the target molecule;

determining the rms (root mean square) deviation of one or more common core positions of said plurality of common core positions from one or more other common core positions of said plurality of common core positions; ~~and~~

forming clusters of ligands from said plurality of ligands according to said rms (root mean square) deviation.; and

rating complementarity of the combinatorial library to the target molecule based on the clusters formed.

12. (Currently amended) The at least one program storage device according to claim 11, wherein ~~said method additionally comprises~~ rating the complementarity of the combinatorial library to the target molecule ~~according to~~is based on the number of ligands in a cluster having a minimum rms (root mean square) deviation relative to the number of ligands in the combinatorial library.

13. (Currently amended) The at least one program storage device according to claim 11, wherein said determining the rms (root mean square) deviation comprises:

placing a grid around a binding site of the target molecule;

for each ligand position, determining a location on the grid corresponding to the center of mass of the common core; and

determining the rms (root mean square) deviation of each common core position from every other common core position having a location on the grid within a predetermined distance.

14. (Previously presented) The at least one program storage device according to claim 11, wherein said forming clusters comprises forming clusters using a single linkage clustering algorithm.

15. (Previously presented) The at least one program storage device according to claim 11, wherein said docking each ligand comprises:

performing a conformational search to generate multiple solution conformations of each ligand;

generating a binding site image of the target molecule, said binding site image comprising multiple hot spots;

matching hot spots of the binding site image to atoms in at least one solution conformation of the multiple solution conformations of each ligand to obtain at least one ligand position relative to the target molecule in a ligand-target molecule complex formation; and

optimizing the at least one ligand position while allowing translation, orientation and rotatable bonds of the ligand to vary, and while holding the target molecule fixed.